

Sildenafil

Cardiology Shared Care Guideline

Specialist Details

Name: _____

Location: _____

Tel: _____

Patient Identifier

Date: _____

Introduction

Licensed indications:

Treatment of adults patients with pulmonary arterial hypertension (PAH) classified as WHO functional class II and III, to improve exercise capacity. Efficacy has been shown in primary (idiopathic) pulmonary hypertension and pulmonary hypertension associated with connective tissue disease.

Treatment of paediatric patients aged 1 to 17 years old with pulmonary arterial hypertension. Efficacy in terms of improvement of exercise capacity or pulmonary haemodynamics has been shown in primary pulmonary hypertension and pulmonary hypertension associated with congenital heart disease. The use of sildenafil for other forms of PAH is not recommended.

Treatment should only be initiated by a physician experienced in treatment of PAH and should be in conjunction with clinical colleagues from one of the recognised national PAH centres.

Adult Dosage and Administration

The licensed adult dose of sildenafil is 20mg orally three times a day.

In line with the NHS England Clinical Commissioning Policy (National policy for the treatment of pulmonary hypertension in adults. July 2015. NHS England/A11/P/c) specialists may recommend that patients are prescribed generic sildenafil 25mg three times a day (off-label use) for dose escalation up to 100mg three times a day. Prescribers should be mindful of the GMC guidance¹ on prescribing a medicine outside its licence: "You should usually prescribe licensed medicines in accordance with the terms of their licence. However, you may prescribe unlicensed medicines where, on the basis of an assessment of the individual patient, you conclude, for medical reasons, that it is necessary to do so to meet the specific needs of the patient." In this situation the responsibility that falls on healthcare professionals when prescribing a medicine off-label may be greater than when prescribing a licensed medicine within the terms of its licence. Prescribers should pay particular attention to the risks associated with using a licensed medicine off-label. In addition, it is recommended that prescribers record the details of the medicine prescribed, the reasons for prescribing this medicine and a record that the issue has been discussed with the patient*.

(1. Good practice in prescribing and managing medicines and devices. GMC. March 2013)

Tablets should be taken approximately 6-8 hours apart, with or without food.

Paediatric dosage and administration:

For paediatric patients aged 1 year to 17 years old, recommended dose for:

Patients ≤ 20 kg is 10 mg (1 ml of 10mg/ml suspension) three times a day.

Patients > 20 kg is 20 mg (2 ml of 10mg/ml suspension or 1 tablet) three times a day.

Neonates and Child 1 month– 1 year: (not licensed)

Initially 250-500 micrograms/kg every 4-8 hours, adjusted according to response; max. 30mg daily. Start with lower dose and frequency especially if used with other vasodilators. (BNFC online)

Higher than recommended doses should not be used in paediatric patients with PAH

Available as:

- Sildenafil 20mg tablets.
- Sildenafil 10mg/ml powder for oral suspension.
- Sildenafil (generic) 25mg tablets (off label use)

Hospital Specialist Responsibilities

- Assess patient's suitability for treatment with sildenafil.
- Arrange shared care with the patient's GP.
- Provide patient/carer with relevant (preferably written) information on use, side-effects and need for monitoring of medication. See also advice above*.

Baseline tests:

• Blood pressure	• LFTs	• U&Es
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- Review results of safety monitoring and request additional tests as required.
- Monitor disease response to treatment and need to continue therapy.
- Continue to review the patient at agreed specified intervals, sending a written summary to the GP whenever the patient is reviewed.
- Provide any other advice or information for the GP including dose adjustments.

GP Responsibilities

- Prescribe sildenafil according to dose advised by specialist.
- Report adverse drug reactions to initiating specialist and usual bodies (e.g. MHRA).
- Ensure no drug interactions with other medicines.

Adverse Effects, Precautions and Contraindications

- **Contraindications include:** Severe hepatic impairment, recent stroke or MI, hypotension (BP < 90/50 mmHg), loss of vision in one eye because of non-arteritic anterior ischaemic optic neuropathy (regardless of whether this episode was in connection or not with previous PDE5 inhibitor exposure), pulmonary hypertension secondary to sickle cell anaemia. Use is not recommended if there are known hereditary degenerative retinal disorders such as *retinitis pigmentosa*.
- **Caution advised with:** males with anatomical deformation of the penis or with a predisposition to prolonged erection (e.g. in sickle-cell disease, multiple myeloma, or leukaemia), autonomic dysfunction, hypotension, volume depletion, pulmonary veno-occlusive disease, or patients taking an alpha blocker due to the possibility of postural hypotension.
- **Commonly reported side effects include:** Dyspepsia, vomiting, diarrhoea, headache, flushing, dizziness, vertigo, vasodilation, myalgia, nasal complaints, dry mouth, haemorrhage, pain in extremity.
- Dose related, transient impairment of blue/green colour vision has been reported, which is consistent with inhibition of PDE6 involved in phototransduction in the retina.
- **Ischaemic optic neuropathy, and raised intra-ocular pressure** have been reported. Patients should be advised in the case of a sudden visual defect to stop taking sildenafil and contact their specialist or GP immediately.
- Hypersensitivity reactions (including rash), priapism, and painful red eyes have been reported.
- Abrupt discontinuation does not seem to be associated with rebound worsening of PAH, but gradual discontinuation with increased monitoring is recommended.
- Use with caution in **Pregnancy**. Due to lack of data, sildenafil should not be used in pregnant women unless strictly necessary.
- **Breast feeding:** It is not known whether sildenafil enters the breast milk. Sildenafil should not be administered to breast-feeding mothers.

Common Drug Interactions

- **Riociguat** in combination with sildenafil is **contraindicated**; may potentially lead to symptomatic hypotension.
- **Potent CYP3A4 inhibitors e.g. ketaconazole, itraconazole, ritonavir:** concomitant use is **contraindicated**
- **Nitrates:** potentiation of hypotensive effects; avoid concomitant use.
- **Nicorandil** is a hybrid of potassium channel activator and nitrate. Due to the nitrate component it has a potential to have serious interaction with sildenafil.
- **Alpha blockers:** concomitant administration of sildenafil to patients taking alpha blocker therapy (e.g. doxazosin) may lead to symptomatic hypotension in susceptible individuals.
- Decrease in dose may be required when sildenafil is administered with intermediate potency CYP3A4 inhibitors (e.g. erythromycin, clarithromycin, nefazodone).
- Dose adjustment may be required when administered with potent CYP3A4 inducers (e.g. carbamazepine, phenytoin, phenobarbital, St John's Wort and rifampicin) or when sildenafil is administered with bosentan, a moderate inducer of CYP3A4.
- The concomitant use of sildenafil and grapefruit juice is not recommended.

Communication

For any queries relating to this patient's treatment with sildenafil, please contact the specialist named at the top of this document.

This information is not inclusive of all prescribing information and potential adverse effects.
Please refer to full prescribing data in the SPC at www.medicines.org.uk or the BNF

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